

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 06 FEB 2004

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Applicant's or agent's file reference JBV/P32975	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/00824	International filing date (day/month/year) 27.01.2003	Priority date (day/month/year) 29.01.2002
International Patent Classification (IPC) or both national classification and IPC C07D513/04		
Applicant GLAXO GROUP LIMITED ET AL.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 12.08.2003	Date of completion of this report 04.02.2004
Name and mailing address of the International preliminary examining authority:  European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Hass, C Telephone No. +49 30 25901-340 

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International application No. **PCT/EP 03/00824**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-39 as originally filed

Claims, Numbers

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
 - ☒ claims Nos. 10 (with regard to industrial applicability)
because:
 - ☒ the said international application, or the said claims Nos. 10 relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - ☐ no international search report has been established for the said claims Nos.
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the Standard.
 - ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-13
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-13
Industrial applicability (IA)	Yes: Claims	1-9, 11-13
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 10 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 Cited documents

- D1: WO 01 07432 A (DAVIES DAVID THOMAS; MARKWELL ROGER EDWARD (GB); LIGHTFOOT ANDREW) 1 February 2001 (2001-02-01) cited in the application
- D2: WO 01 07433 A (MARKWELL ROGER EDWARD; PEARSON NEIL DAVID (GB); SMITHKLINE BEECHAM) 1 February 2001 (2001-02-01) cited in the application
- D3: WO 00 78748 A (DAVIES DAVID THOMAS; MARKWELL ROGER EDWARD (GB); PEARSON NEIL DAVI) 28 December 2000 (2000-12-28) cited in the application
- D4: WO 00 21948 A (HATTON IAN KEITH; PEARSON NEIL DAVID (GB); SMITHKLINE BEECHAM PLC) 20 April 2000 (2000-04-20) cited in the application
- D5: WO 00 43383 A (DAVIES DAVID THOMAS; HENRY CAROLINE JOAN (GB); PEARSON NEIL DAVID) 27 July 2000 (2000-07-27) cited in the application
- D6: WO 00 21952 A (DAVIES DAVID THOMAS; MARKWELL ROGER EDWARD (GB); PEARSON NEIL DAVI) 20 April 2000 (2000-04-20) cited in the application
- D7: WO 99 37635 A (COATES WILLIAM JOHN; MASTERS PHILIP JOHN (GB); WARRACK JULIE DOROT) 29 July 1999 (1999-07-29) cited in the application

V.2 Novelty

The subject-matter of claim 1 is different from D1 at least with regard to the substituent R³ at the piperidine ring.

The subject-matter of claim 1 differs from documents D2 to D7 at least due to the substituent R^4 , which bears a bicyclic ring system. None of these documents mention concrete compounds having (in the R^4 -corresponding portion) such a ring system as substituent.

The subject-matter of claims 1-13 is thus regarded novel with regard to D1-D7.

V.3 Inventive step

V.3.1 According to the description, the problem underlying the present application can be seen in the provision of further aminopiperidine derivatives which are useful in the treatment of bacterial infections.

V.3.2 Re inventive step, all of the cited prior art documents are relevant since they all disclose structurally related compounds also being antibacterially active. D1 is considered to represent the most relevant prior art since the D1 compounds are different from the present ones only with regard to the radical R^5 which is a part of the substituent R^4 ; and they are different with regard to the substituent R^3 , which can be oxo, trifluoromethyl, fluorine and amino or substituted amino in the present compounds, but which is carboxy, alkoxycarbonyl, aminocarbonyl, substituted aminocarbonyl, or alkyl or ethenyl (which can be substituted) in D1.

V.3.3 The overall disclosure of D1 comprises, as possibilities of the R^5 group, a number of possibilities including "optionally substituted heteroaryl" (see D1, claim 1, definition of R^5). According to the definition given in D1, page 6, line 28 to page 7, line 10, "heteroaryl" includes aromatic heterocyclic groups which can be single or fused rings; as fused rings, quinoliny and benzothiény are explicitly mentioned. So the only relevant structural difference between the present compounds and the compounds of D1 appears to reside in the substituent R^3 (see paragraph "Novelty" above). The R^3 group in D1 can be cyano, which is chemically related to the halogens, and the R^3 in D1 can additionally be (C_{1-4}) alkyl substituted with R^{12} groups which can e.g. be halogen. It is true that such possibilities are only generically disclosed in D1, however, by these listings in D1, the structural modifications of the present compounds, compared with the possibilities disclosed in D1, must be considered obvious since they are foreshadowed in D1. Moreover, the compounds of the present application apparently exhibit the same technical effect as the D1 compounds, namely an antibacterial activity. Consequently, at the moment, the presence of an inventive step must be denied for the subject-matter

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of compound claims 1-9 as well as for the subject-matter of the pharmaceutical claims 10-12. This conclusion correspondingly applies to process claim 13, which claims a process that is analogous to the process disclosed in D1, page 8, line 32 to page 9, line 31. It follows that the subject-matter of claim 13 is not inventive either.

V.3.4 Inventive step, however, could have been acknowledged if the applicant had made credible that with the present compounds a more exacting problem is solved (e.g. provision of compounds which have a better activity compared to the D1 compounds) so that the solution of this problem could be regarded as non-obvious. However, no such arguments have been submitted by the applicant.

V.4 Industrial applicability

V.4.1 The subject-matter of claims 1-9 and 11-13 is considered to be industrially applicable.

V.4.2 For the assessment of the present claim 10 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

V.5 Miscellaneous

Page 1, line 5: WO 00/25227 is apparently cited erroneously since it does not deal with any chemical matter. The correct citation seems to be "WO 01/25227".